Docket No. GP-100C1
Serial No. 08/860,844

Remarks

Claims 28, 29, 49 and 52-61 were previously pending in the subject application. By this Amendment, claims 28 and 57 have been amended, claims 29, 49, 52-56, and 59-61 have been canceled and new claims 62-65 have been added. Accordingly, claims 28, 57, 58 and 62-65 are before the Examiner for his consideration. Support for these amendments can be found throughout the subject specification and in the previous claims. The amendments to the claims have been made in an effort to lend greater clarity to the claimed subject matter and to expedite prosecution. These amendments should not be taken to indicate the applicants' agreement with, or acquiescence to, the rejections of record. Favorable consideration of the claims now presented, in view of the remarks and amendments set forth herein, is earnestly solicited.

As an initial matter, the Office Action indicates that a new title is required. By this Amendment, the applicants have amended the title of the subject application.

The applicants wish to thank the Examiner for his careful consideration of the claims submitted with the applicants' amendment dated August 26, 2002. The applicants particularly wish to express their appreciation for the Examiner's indication that claims 29 and 56-58 have only been objected to, and that these claims would be allowable if re-written in independent form including all of the limitations of the base claim and any intervening claims.

In this regard, previous claim 28 has been amended herein to include the limitations of claim 29. Accordingly, claim 29 has now been cancelled and the applicants respectfully submit that claim 28, as amended, should be allowable.

Further, new claim 62 has been presented herein. This new claim is based on previous claim 56. Thus, previous claim 56 has now been cancelled and the applicants respectfully submit that new claim 62 should be allowable (as should dependent claims 57 and 58).

Further, new claim 63 has been presented herein. This claim is based on previous claim 59 (which was, also, only objected to). Please note that in drafting new claim 63 the applicants have eliminated reference to the "downregulation" of the gene. In the outstanding Office Action the Examiner noted that reference to "downregulation" in claim 59 might be misinterpreted to refer to an effect on gene expression. Accordingly, in new claim 63, the applicants more clearly recite that the recognition unit has been modified to reduce its binding affinity. The applicants appreciate the

Examiner's identification of this issue and respectfully submit that new claim 63 should be allowable.

Accordingly, claims 28, 57, 58 and 62-63 presented herein are intended to set forth subject matter already indicated as being allowable in the outstanding Office Action. Therefore, the applicants respectfully request allowance of these claims upon review by the Examiner.

Finally, the applicants have also presented new claims 64 and 65. The purpose of these claims is to describe the claimed subject matter in greater detail and with great specificity (compared to the claims in the applicants' previous amendment) so as to most clearly distinguish the claimed subject matter from the previously-cited Frankel *et al.* and Essignmann *et al.* references.

Thus, in claim 64 the applicants have endeavored to strongly emphasize the critical attributes of the subject invention whereby TBAs are designed to have multiple nucleic acid recognition units that function cooperatively so that binding occurs only to a specific target sequence, and that an advantageous therapeutical effect results from this binding. The recitation of a design step is in accordance with the Examiner's observation at page 4 (end of the first paragraph) of the outstanding Office Action.

Claim 65 is drawn to a specific, highly advantageous, embodiment of the subject invention wherein the constructs comprise assembly sequences in addition to the nucleic acid recognition units. The use of assembly sequences is described in detail throughout the subject application. See, for example, page 29 line 24 to page 30 line 9 wherein assembly sequences are discussed generally, and specific examples are given. See also, page 30, lines 24-26; page 38, lines 11-18; page 43 lines 8-9; and page 53 line 23 to page 54 line 19. As disclosed in the subject specification, the use of assembly sequences can greatly enhance the specificity of the constructs of the subject invention. Note, for example, page 34, lines 28-30 where it is noted that:

> One feature of the multimeric assembly of TBAs which is specifically claimed here as part of this invention is that such a multimeric assembly is expected to have a much reduced affinity for a single site within the TNA.

As emphasized throughout the prosecution of the subject application, this diminished affinity for individual sites within a target sequence makes it possible for the claimed constructs to be highly

specific because they only bind to a sequence if all of the necessary individual sites are present and in the correct order.

Previous claims 28, 52-54, 60 and 61 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Frankel *et al.* (U.S. Patent No. 5,674,980). Also, previous claims 49 and 55 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Essigmann *et al.* (U.S. Patent no. 5,882,941). To the extent that these references might be applied to new claims 64 and 65, the applicants respectfully request reconsideration.

In their previous response, the applicants emphasized that, in contrast to Frankel *et al.*, the applicants' molecules comprise a plurality of nucleic acid recognition units that work cooperatively for binding to occur. As noted in new claim 64:

> there is sufficient affinity for binding to occur between said TBA and a double stranded nucleic acid molecule only if all of the specific individual target nucleic acid sequences are present, and in the order and location corresponding to said target double stranded nucleic acid molecule. (emphasis added)

The Office Action notes that a Frankel *et al.* construct utilizes the E2 region and that this region has both positive and negative acting transcriptional regulators. Although these transcriptional regulators presumably bind to certain nucleotide sequences, the applicants see no indication that the binding of both of these sequences is necessary (as required by the current claims) in order for binding to occur to a target sequence.

With regard to the applicants' emphasis on the different function of the Frankel *et al.* construct compared to the applicants' system, the reason this is important is that, because these technologies are for different purposes, there would be no reason to modify the Frankel *et al.* system to arrive at the currently-claimed invention.

With regard to Essigmann *et al.*, the applicants respectfully submit that the cooperative binding of the applicants' system (as emphasized in claim 64) is not disclosed or suggested by the Essigmann *et al.*

As noted above, new claim 64 also recites a design step, further distinguishing the claimed subject matter from the cited references. Also, claim 65 is drawn to a specific embodiment comprising assembly sequences where the nucleic acid binding domains are not simply ligated

together, but only assemble to become an effective TBA when bound in the target sequence. Such constructs are not disclosed or suggested by the cited references.

Accordingly, to the extent that Frankel *et al.* and Essigmann *et al.* might be applied to new claims 64 and 65, the applicants respectfully submit that the subject matter of claims 64 and 65 is neither anticipated by, nor obvious in view of, these references.

In view of the foregoing remarks and the amendments above, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

The applicant also invites the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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DRS/la
Attachment: Marked-up Version of Amended Claims

Marked-up Version of Substituted Claims

Claim 28 (five times amended):

28. A method of using a target binding assembly (TBA) wherein said TBA comprises a plurality of nucleic acid recognitions units wherein each of said nucleic acid recognition units binds to a specific nucleic acid sequence on a target double stranded nucleic acid molecule; and wherein the combined binding affinity of said plurality of nucleic acid recognition units is such that said TBA specifically binds to the target double stranded nucleic acid molecule but does not bind to non-target molecules; and wherein said method comprises administering to a patient a therapeutically or prophylactically effective amount of said TBA, or nucleic acid which codes for and produces said TBA, such that the TBA binds a target double stranded nucleic acid molecule to achieve a desired prophylactic or therapeutic result; and wherein said TBA is selected from the group consisting of SEQ ID NO. 109, SEQ ID NO. 110, SEQ ID NO. 111, SEQ ID NO. 112, SEQ ID NO. 113, SEQ ID NO. 114, SEQ ID NO. 115, and SEQ ID NO. 116, and the patient is infected with HIV or HPV.

Claim 57 (amended):

57. The method, according to claim [56] 62, wherein one of said nucleic acid recognition units comprises a DNA-binding portion of NF-kB.